



Nordic mcl2-3 trials: mirna-18b overexpression identifies a mantle cell lymphoma subgroup with poor survival and improves mipi-b prediction of prognosis

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Health economics

P1268

COST-EFFECTIVENESS OF EDOXABAN, APIXABAN, RIVAROXABAN AND DABIGATRAN VERSUS WARFARIN FOR STROKE PREVENTION IN NONVALVULAR ATRIAL FIBRILLATION

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Background: Non-valvular atrial fibrillation (NVAF) causes one fifth of overall ischemic strokes, therefore, oral anticoagulation with warfarin is recommended since it can prevent about one third of the events. Novel oral anticoagulants (NAO), *i.e.* oral inhibitors of thrombin or factor Xa, compete with warfarin in this setting since a simplified monitoring is required and intracranial bleedings are significantly reduced.

Aims: We aimed at assessing the cost-effectiveness of NAOs (dabigatran, apixaban, rivaroxaban, edoxaban), *versus* warfarin, for stroke prevention in NVAF patients with CHADS2 score ≥ 2 .

Methods: We built a Markov decision model including 11 health-states. Quarterly transition probabilities among states were estimated based on data from published randomized trials. Quality of life estimations for each event or health-state were derived from reference studies. For each therapeutic strategy, the model estimated expected quality-adjusted life-years (QALY) in the lifetime horizon. The economic analysis was performed in the perspective of the Italian National Health System. Quarterly drug cost of NAOs was €198 *versus* €3.9 of warfarin. Future life years and costs were discounted by 3.5% per year, according to international guidelines. Incremental cost per QALY gained (ICUR) as compared with warfarin was calculated for each NAO. First- and second-order (probabilistic) sensitivity analyses were run. The model was developed and run by TreeAge SW.

Results: NAOs increased quality-adjusted life expectancy by 0.405-0.753 discounted years, as compared with warfarin. Incremental lifetime health-care costs of patients assigned to NAOs ranged from €3,439 to €4,923. The cost-effectiveness of NAOs *versus* warfarin ranged from €4,567/QALY (80%CI: 2,129-8,993) for apixaban to €12,156/QALY (80%CI: 5,147-33,200) for rivaroxaban. Dabigatran and edoxaban reported intermediate ICUR values: €6,307/QALY (80%CI: 3,034-13,421) and €7,713/QALY (80%CI: €3,909-€17,963), respectively. Second-order sensitivity analysis showed that the results were robust: over 90% of the simulations provided an incremental-cost-effectiveness ratio lower than €50,000/QALY, irrespectively of the NAO being compared with warfarin. The results were sensitive to the time in warfarin therapeutic range, the analysed time horizon, and the impact of anticoagulants onto quality of life. NAO cost variation by 20% induced ICUR variations by about €3,000/QALY.

Summary and Conclusion: NAOs are cost-effective drugs for stroke prevention in moderate-high risk patients with NVAF. Lacking head-to-head studies, the relative cost-effectiveness of one NAO *versus* another one is surrounded by a wide uncertainty. Economic sustainability of widespread NAO adoption in industrialized countries still needs to be assessed, therefore phase 4 studies should investigate clinical and economic outcomes in specific patient subgroups, *i.e.* warfarin-treated patients with a high rate of time-in-treatment-range.

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ECONOMIC VALUE CREATED BY ADDING RITUXIMAB TO CHEMOTHERAPY IN THE UNITED STATES FROM 1998-2013

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Background: Rituximab has become the standard in diffuse large B-cell lymphoma (DLBCL), follicular lymphoma (FL), and chronic lymphocytic leukemia (CLL). The incremental cost of adding rituximab to existing chemotherapy and the value of the life years saved have not been estimated at the population level.

Aims: Our objective is to estimate the net economic value of rituximab in the United States for policy decision-makers.

Methods: We constructed a population effectiveness model from 1998-2013. Age group, gender, and year-specific incidence rates for each cancer were estimated from the Surveillance, Epidemiology, and End Results (SEER) program. Incidence rates were multiplied by Census estimates to calculate total diagnosed patient counts. Utilization, survival and cost inputs were estimated using SEER Medicare merged data for patients diagnosed 1999-2009 and followed through 2010, extrapolated through 2013. First-line utilization of rituximab plus chemotherapy (R+Chemo) and Chemo Alone were calculated as a proportion of all diagnosed patients to estimate treated patient counts.

Differences in mean survival between R+Chemo and Chemo Alone for each cancer were estimated using flexible parametric survival models. The incremental cost of R+Chemo *versus* Chemo Alone for each cancer was based on Medicare paid amounts for all Part A and B services using regression, accounting for censoring. Costs were computed over 72-months to capture short and long-term effects, and inflated to 2013 US dollars. The value of a life year saved (\$90,941 in 2013 dollars) was based on published literature (Lee, *et al.* 2009). Monte Carlo sampling was used to estimate the 95% uncertainty intervals (UI).

Results: Across all three cancers from 1998 to 2013, there were 280,819 cumulative life years saved (95% UI, 269,136-293,345). The additional total costs of care for R+Chemo were \$33,525, \$23,511, and \$31,435 in DLBCL, FL, and CLL, respectively. Across all 3 tumors, the incremental direct medical cost of R+Chemo compared to Chemo Alone was \$7.0 billion (95% UI \$5.8-\$8.2 billion), and the resulting economic value of the life years saved was \$25.5 billion (95% UI \$11.7-\$69.1 billion).

Summary and Conclusion: For DLBCL, FL and CLL patients treated with R+Chemo in the US from 1998-2013, 281,000 life years were saved that created a net economic value of \$18.5 billion.

P1270

COST-EFFECTIVENESS ANALYSIS OF BENDAMUSTINE PLUS RITUXIMAB AS FIRST-LINE TREATMENT FOR PATIENTS WITH FOLLICULAR LYMPHOMA. PRELIMINARY RESULTS

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Background: Follicular lymphoma (FL) is the most common type of indolent non-Hodgkin's lymphomas (NHL), and despite substantial improvement in survival, it is usually incurable in most cases. The disease characteristically responds well to first-line therapy but typically manifests repeated relapses with the need of recurrent therapeutic interventions, with disease-free intervals. Patients with FL in advanced stages and high-tumour burden usually receive front-line chemoimmunotherapy, rituximab (R) + chemotherapy, during the so called induction phase, followed by maintenance therapy with R in patients who achieve at least a partial response after the induction phase, as it is recommended by several Clinical Guidelines.

Aims: To evaluate the cost-effectiveness of rituximab-bendamustine (R-B) compared with R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone) as first-line treatment for patients with advanced FL in Spain.

Methods: A Markov model was built to simulate a patient cohort with FL during a time horizon of 25 years (4 weeks-cycle length). Clinical data were adapted from two phase III randomized trials, one with the FL patients analyzed by the German Study group indolent Lymphomas (StiL) which compared R-B with R-CHOP during the induction phase, followed by the data obtained in the PRIMA trial during the maintenance therapy with R. Four health states were considered: progression-free survival (including induction and maintenance), first relapse, second relapse and death. Transition probabilities were obtained from progression-free survival curves available in the literature. Mortality rates were obtained from GLOBOCAN registry and from recently published epidemiological data after the "rituximab era". The Study Perspective was the Spanish National Health System (NHS) and only direct healthcare costs were considered. Resources consumed during patients treatment and follow-up where identified by panel of Spanish experts in FL. Unitary costs were obtained from the Drug Catalogue and e-Salud Database. Drug costs were calculated based on ex-factory prices with mandatory 7.5% rebate. All costs were updated to € 2013. Utilities for each health state were obtained from the literature. The final efficacy measure was quality-adjusted life-years (QALYs). Costs and health outcomes were discounted at a 3% annual discount rate. To check for the robustness of the results, a probabilistic sensitivity analysis was performed with 10,000 Monte Carlo simulations.

Results: The initial treatment and administration costs during the induction phase were higher with R-B (€16,481.63) compared to R-CHOP (€10,793.97). Nevertheless, at the end of the 25 year period, in the deterministic analysis, and considering only the GLOBOCAN registry mortality rate, R-B first line strategy accounted a total cost of €686,848.46 compared to €725,450.80 for R-CHOP. Health benefits measured as QALYs was higher in R-B with 14.25 QALYs than in R-CHOP with 13.95 QALYs. In the probabilistic analysis, R-B was a dominant strategy compared to R-CHOP in 99.9% of the simulations.